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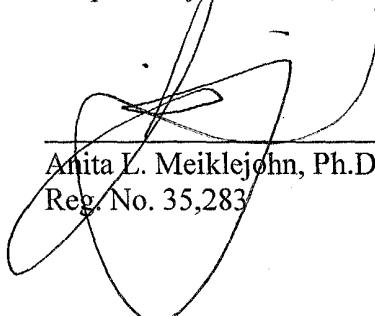
Attorn[redacted]s Docket No.: 11926-015001

REMARKS

The amendment to the specification is made solely to insert the Sequence Listing and SEQ ID NOS. into the specification. No new matter is introduced. The accompanying declaration by the inventor (unsigned) confirms that the sequences in the Sequence Listing are the same as those incorporated by reference into the original specification by providing the GenBank® Accession Number for each sequence. A signed copy of the declaration will be submitted shortly.

Attached is a marked-up version of the changes being made by the current amendment.  
Please apply any other charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

  
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Version with markings to show changes made

In the specification:

Table 10 beginning at page 171 has been amended as follows:

Table 10  
Variance Table

Hugo Variance	GID Start	OMIM ID	VGX Symbol	Description
U73338	U73338	156570	GEN-69	Methionine
<u>Synthase (SEQ ID NO:1)</u>				
194		(-201)C>G	5'	
284		(-111)C>T	5'	
1136		742G>A	V248M	
1252		858C>T	Silent	
1334		940G>A	D314N	
1699		1305T>C	Silent	
3150		2756A>G	D919G	
3207		2813G>T	S938I	
3209		2815G>C	G939R	
5444		5050C>A	3'	
5551		5157G>A	3'	
5573		5179C>T	3'	
5659		5265T>C	3'	
5678		5284T>C	3'	
5874		5480C>T	3'	
5934		5540A>G	3'	
D78586	D78586	114010	GEN-BR	CAD PROTEIN (SEQ ID NO:2)
3434		3408C>T	Silent	
4313		4287T>C	Silent	
4799		4773A>G	Silent	
5255		5229C>T	Silent	
5455		5429G>A	R1810Q	
5507		5481T>C	Silent	
5810		5784C>T	Silent	
6128		6102C>T	Silent	
6626		6600C>T	Silent	
6686		6660C>T	Silent	
U09178	U09178	274270	GEN-HA	
<u>Dihydropyrimidine Dehydrogenase (SEQ ID NO:3)</u>				

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166	85T>C	C29R		
577	496A>G	M166V		
638	557A>G	Y186C		
1708	1627A>G	I543V		
3432	3351T>C	3'		
3682	3601C>T	3'		
3730	3649G>A	3'		
3925	3844A>G	3'		
3937	3856T>C	3'		
U19720	U19720	600424	GEN-II	Folate
Transporter	(SLC19A1)	(SEQ ID NO:4)		
175	80G>A	R27H		
341	246C>G	Silent		
791	696C>T	Silent		
1067	972G>A	Silent		
1337	1242C>A	Silent		
1997	1902T>C	3'		
2100	2005^2006insG	3'		
2582	2487T>G	3'		
2617	2522C>T	3'		
2652	2557T>C	3'		
U92868	U92868	600424	GEN-LUK	Homo sapiens reduced
folate carrier (RFC1) gene, exons 1a, 1c and 1b	(SEQ ID NO:5)			
431	431A>G	Intron		
441	441A>G	Intron		
498	498C>T	Intron		
579	579G>C	Intron		
599	599G>C	Intron		
X02308	X02308	188350	GEN-KL	Thymidylate
synthetase	(SEQ ID NO:6)			
1066	961T>C	3'		
1136	1031A>G	3'		
1497	1392T>A	3'		
D00517	D00517	188350	GEN-LUC	Thymidylate
synthase, promoter	(SEQ ID NO:7)			
276	276C>T	Intron		
321	321T>C	Intron		
452	452G>A	Intron		
457	457^insC	Intron		
491	491C>A	Intron		
533	533T>C	Intron		
624	624A>C	Intron		
639	639A>G	Intron		
655	655T>C	Intron		

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D00596 D00596 188350 GEN-LUD Homo sapiens  
gene for thymidylate synthase, exons 1, 2, 3, 4, 5, 6, 7,  
complete cds (SEQ ID NO:8)

701	701A>C	Intron
716	716A>G	Intron
732	732T>C	Intron
1293	1293A>G	Intron
1322	1322C>G	Intron
1379	1379T>C	Intron
1590	1590C>T	Intron
1688	1688C>G	Intron
2401	2401A>G	Intron
2429	2429G>A	Intron
2488	2488C>T	Intron
2594	2594G>T	Intron
2618	2618G>A	Intron
3083	3083G>A	Intron
3125	3125G>A	Intron
3212	3212C>T	Intron
3619	3619T>A	Intron
3635	3635G>A	Intron
4256	4256G>A	Intron
4898	4898A>G	Intron
5006	5006C>T	Intron
5062	5062G>A	Intron
5167	5167G>A	Intron
11069	11069A>G	Intron
11238	11238C>T	Intron
11293	11293T>G	Intron
11422	11422T>C	Intron
11686	11686C>T	Intron
12598	12598T>C	Intron
13171	13171T>C	Intron
13298	13298G>A	Intron
13645	13645T>C	Intron
13751	13751C>A	Intron
13782	13782T>C	Intron
13806	13806T>C	Intron
13813	13813T>C	Intron
14479	14479A>G	Intron
14546	14546^inst	Intron
14585	14585C>T	Intron
14729	14729G>A	Intron
14787	14787C>T	Intron
14795	14795G>A	Intron

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15041	15041T>C	Intron		
15343	15343G>A	Intron		
15449	15449G>A	Intron		
15502	15502G>A	Intron		
15545	15545C>T	Intron		
15589	15589A>G	Intron		
15769	15769C>T	3'		
15839	15839A>G	3'		
16148	16148G>A	3'		
16198	16198T>G	3'		
16202	16202G>T	Intron		
X59618	X59618	180390	GEN-M3	Ribonucleotide
reductase M2 polypeptide		(SEQ ID NO:9)		
128	(-67)G>A	5'		
189	(-6)T>G	5'		
524	330C>G	Silent		
1399	1205T>A	3'		
1464	1270G>A	3'		
1636	1442C>T	3'		
1738	1544C>T	3'		
2259	2065T>C	3'		
S72487	S72487	131222	GEN-3LD	Thymidine
phosphorylase, partial		(SEQ ID NO:10)		
183	19G>A	D7N		
483	319C>T	3'		
601	437G>C	3'		
1299	1135G>A	3'		
M58602	M58602	131222	GEN-LUB	Thymidine
phosphorylase, promoter and genomic		(SEQ ID NO:11)		
124	124C>T	3'		
439	439G>A	3'		
1044	1044^insCT	3'		
1331	1331G>A	3'		
1977	1977G>A	Intron		
2149	2149G>A	Intron		
2467	2467A>G	Intron		
2634	2634C>G	Intron		
2975	2975G>A	Intron		
3116	3116G>T	Intron		
3255	3255A>C	Intron		
3344	3344T>C	Intron		
4051	4051C>A	Intron		
4782	4782G>A	Intron		
5022	5022T>C	Intron		
5266	5266G>A	Intron		

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5285	5285C>G	Intron
5438	5438T>A	Intron
5482	5482C>T	Intron
5629	5629G>A	Intron
5648	5648C>T	Intron
5731	5731G>A	Intron
M98045	M98045	136510 GEN-4C3 Homo sapiens
folylpolyglutamate synthetase mRNA, complete cds <u>(SEQ ID NO:12)</u>		
802	732C>T	Silent
1747	1677G>T	3'
1900	1830T>C	3'
U24253	U24253	136510 GEN-LUE Human
folylpolyglutamate synthetase (FPGS) gene, exons 5-11, and		
partial cds <u>(SEQ ID NO:13)</u>		
1424	1424C>A	Intron
1649	1649G>A	Intron
2554	2554A>G	Intron
U24252	U24252	136510 GEN-LUF
Folylpolyglutamate synthetase, promoter and exons 1-4 <u>(SEQ ID</u>		
<u>NO:14)</u>		
263	263A>G	Intron
266	266G>T	Intron
527	527C>G	Intron
1037	1037A>G	5'
1139	1139G>A	Intron
1217	1217C>T	Intron
1647	1647C>T	Intron
1955	1955G>A	Intron
2017	2017G>A	Intron
2037	2037G>A	Intron
2189	2189A>G	Intron
2282	2282C>T	Intron
2309	2309A>G	Intron
U09806	U09806	236250 GEN-4FZ Human
methylenetetrahydrofolate reductase mRNA, partial cds <u>(SEQ ID</u>		
<u>NO:15)</u>		
120	120T>C	Silent
464	464T>G	M155R
519	519C>T	Silent
668	668C>T	A223V
1059	1059T>C	Silent
1289	1289C>A	3'
1308	1308T>C	3'
1784	1784G>A	3'

AF061655	AF061655	123920	GEN-LUJ	Cytidine
deaminase, promoter		<u>(SEQ ID NO:16)</u>		
575		575T>C	Intron	
648		648T>C	Intron	
771		771G>C	Intron	
883		883G>A	Intron	
941		941^insC		5'
1051		1051A>C		K27Q

In the Claims

Claims 171, 172, and 181 have been amended as follows.

171. An isolated nucleic acid probe comprising at least 15 contiguous nucleotides of the nucleotide sequence of SEQ ID NO:15 (methylenetetrahydrofolate reductase), the probe comprising at least one of:

- (a) nucleotide 120 wherein [X] N is C;
- (b) nucleotide 464 wherein [X] N is G;
- (c) nucleotide 519 wherein [X] N is T;
- (d) nucleotide 668 wherein [X] N is T;
- (e) nucleotide 1059 wherein [X] N is C;
- (f) nucleotide 1289 wherein [X] N is A;
- (g) nucleotide 1308 wherein [X] N is C;
- (h) nucleotide 1784 wherein [X] N is A;

or the complement thereof.

172. The isolated nucleic acid probe of claim 171 comprising at least two of:

- (a) nucleotide 120 wherein [X] N is C;
- (b) nucleotide 464 wherein [X] N is G;
- (c) nucleotide 519 wherein [X] N is T;
- (d) nucleotide 668 wherein [X] N is T;
- (e) nucleotide 1059 wherein [X] N is C;
- (f) nucleotide 1289 wherein [X] N is A;
- (g) nucleotide 1308 wherein [X] N is C;
- (h) nucleotide 1784 wherein [X] N is A;

or the complement thereof.

181. A method comprising:

(a) providing a sample comprising nucleic acid molecules present in a biological sample obtained from a patient;

(b) contacting the sample with a probe comprising at least 15 contiguous nucleotides of the nucleotide sequence of SEQ ID NO:15 (methylenetetrahydrofolate reductase), the probe comprising at least one of:

- (i) nucleotide 120 wherein [X] N is C;

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- (ii) nucleotide 464 wherein [X] N is G;
- (iii) nucleotide 519 wherein [X] N is T;
- (iv) nucleotide 668 wherein [X] N is T;
- (v) nucleotide 1059 wherein [X] N is C;
- (vi) nucleotide 1289 wherein [X] N is A;
- (vii) nucleotide 1308 wherein [X] N is C;
- (viii) nucleotide 1784 wherein [X] N is A;

or the complement thereof; and

(c) determining if the sample comprises a nucleic acid molecule that hybridizes to the probe.

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